PATENT
2257-1-001

REMARKS

At the outset, the Applicant would like to thank the Examiner for his helpful comments on December 13, 1999. This Response is being filed in view of these comments. The Applicant also notes that the Examiner has withdrawn the Rejections under 35 U.S.C.§ 112, first and second paragraph and the rejections under 35 U.S.C.§§ 102 and 103 in view of Dullforce. Therefore, the only remaining rejection is under 35 U.S.C.§103. Reconsideration of this Application is respectfully requested.

Rejection under 35 U.S.C. § 103:

The Examiner has maintained the rejection of Claims 1-10, 12, 13, and 15-23 as being obvious over Aruffo *et al.*, and/or Armitage *et al.*, and/or Ledbetter *et al.*, in view of Noelle, Mond *et al.*, Scott *et al.*, and Marburg *et al.* The Examiner asserts that Aruffo *et al.*, and/or Armitage *et al.*, and/or Ledbetter *et al.*, use CD40 ligand or CD40-specific antibodies as adjuvants for vaccines to boost immune responses in various individuals. The Examiner admits that these references differ from the present Invention by not disclosing all of the methods and formulations of making the vaccines which comprise an adjuvant nor do they disclose the combination of an adjuvant with an antigen of interest. However, the Examiner asserts that the combination of an adjuvant with an antigen of interest was known in the art. Further, the Examiner asserts that vaccine formulations and methods of making the vaccines were all known at the time the invention was made. The Examiner further asserts that there were various means to make and formulate the vaccines for a number of antigens including both TD and TI antigens. The Examiner finally asserts that the constructs comprising immunogenic compositions comprising an adjuvant and an antigen in which the adjuvant and antigen are joined together were also known.

The Applicant respectfully traverses the Examiner's rejections. The Examiner admits that the present invention as claimed is novel. However, the Examiner asserts that there is a

reasonable expectation of success for the present invention provided by the cited literature. The present invention, however, is not an obvious extension of the current immunological dogma. Indeed, a conjugate of the CD40 antibody and a given antigen would not be expected to be effective in enhancing immune responses. For example, it would be anticipated that the antigen-anti-CD40 conjugate would be internalized by antigen presenting cells and then processed into short peptides for preparation of MHC class II presentation. Since the anti-CD40 antibody would be proteolyzed along with the antigen in the APC, the anti-CD40 antibody would be expected to be unable to stimulate B cells through the CD40 receptor.

Neither Aruffo *et al.*, *nor* Armitage *et al.*, nor Ledbetter *et al.* teach the invention as claimed. Indeed, neither Aruffo *et al.*, *nor* Armitage *et al.*, nor Ledbetter *et al.* disclose the linking or co-joining of the antigen to the adjuvant taught by the present invention. Therefore, the Examiner is forced to cure the deficiencies of Aruffo *et al.*, Armitage *et al.*, and Ledbetter *et al.* with additional teachings. In an attempt to provide such teachings, the Examiner cites Noelle, Mond *et al.*, Scott *et al.*, and Marburg *et al.* However, Noelle, as the Examiner has previously pointed out, is simply a review article that teaches the importance of CD40 and the CD40 ligand in host defense against a wide variety of antigens. Therefore, Noelle cannot cure the deficiencies of the above-cited art. Neither can Scott *et al.* who only teach the use of a cytokine, interleukin-12, in vaccine formulations for a variety of antigens. Mond *et al.* merely disclose a conjugated dual carrier immunogenic construct having at least one primary carrier that is a T dependent antigen comprising a large molecular weight molecule of greater than a 2000 kilodaltons (such as dextran), and a secondary carrier that is a T independent antigen, (such as diphtheria toxid). Clearly, Mond *et al.* do not lead the skilled artisan to the present invention. Finally, the Examiner has cited Marburg *et al.* However, Marburg *et al.* disclose a particular immunocarrier linked to pure capsular polysaccharide from *Streptococcus* to prevent pneumonia. Indeed, Marburg *et al.* specifically teach a partially hydrolyzed and highly purified antigenically type-specific pneumococcal capsular polysaccharide that is to be used as an intermediate in the preparation of T-cell dependent conjugates of the pneumococcal capsular polysaccharide with antigenic proteins. Therefore, neither Noelle, nor Mond *et al.*, nor Scott *et al.*, nor Marburg *et*

al. lead one of ordinary skill in the art to the present invention, either alone or in any combination including in combination with Aruffo *et al.*, and/or Armitage *et al.*, and/or Ledbetter *et al.*

Consistently, as stated previously, even a recent attempt by researchers from Stanford University to use CD40L as an adjuvant did not include the step of cross-linking the antigen to CD40L [Wong *et al.*, *J. Immunology* **162**:2251-2258 (1999)]. Indeed, the present invention as claimed can only be derived from the blueprint from the Applicant's own disclosure. Therefore the present invention is neither taught nor made obvious by Aruffo *et al.*, Armitage *et al.*, Ledbetter *et al.*, alone or in combination, or in further combination with Noelle, Mond *et al.*, Scott *et al.*, and/or Marburg *et al.*

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully solicited.

In view of the foregoing amendments and remarks, reconsideration and early allowance of Claims 1-10, 12, 13, and 15-23 are respectfully requested.

No additional fees are believed to be necessitated by the foregoing amendments. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages. Should the Examiner feel that a telephone conference would facilitate resolution of any of the above issues, he is invited to telephone the undersigned attorney.

PATENT
2257-1-001

In view of the above and foregoing, reconsideration and withdrawal of the outstanding grounds of rejection and early allowance of the claims as amended is believed to be in order and are respectfully solicited.

Respectfully submitted,

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PATENT
2257-1-001

PENDING CLAIMS

1. (Twice Amended) An immunogenic composition comprising an adjuvant and an antigen; wherein said adjuvant and said antigen are joined together; wherein said adjuvant is selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand; and

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell.

2. (Amended) A vaccine including the immunogenic composition according to Claim 1.

3. (Amended) A vaccine according to Claim 2 wherein said antigen is a T-cell dependent or T-cell independent antigen, or part of said T-cell dependent or T-cell independent antigen.

4. (Amended) A vaccine according to Claim 2 wherein said adjuvant is a CD40 ligand.

5. (Amended) A vaccine according to Claim 2 wherein said adjuvant is an antibody raised against said CD40, or a part of said antibody that is effective at binding CD40.

6. A vaccine according to Claim 5 wherein the antibody is monoclonal.

7. A vaccine according to Claim 5 wherein the antibody is humanised.

8. A vaccine according to Claim 3 wherein said antigen is soluble.

9. A vaccine according to Claim 3 wherein said antigen is a protein.

10. A vaccine A method wherein said antigen is a polysaccharide.

12. (Amended) A vaccine according to Claim 3 wherein said antigen is a protein or part thereof, and said antigen is fused to said adjuvant so as to provide a fusion protein.

13. (Amended) A vaccine according to Claim 2 further comprising at least one cytokine.

15. (Amended) A method for the manufacture of a vaccine capable of enhancing immunity comprising

(a) selecting a suitable T-cell dependent and/or T-cell independent antigen, or parts thereof, and

(b) associating or combining said antigen with an adjuvant; wherein said adjuvant is adapted to stimulate B-lymphocyte receptor, CD40.